

Claims

1. The use of the KDR/Flk-1 epitope Y1214 as a marker in the measurement of a change in the activation state of the KDR/Flk-1 receptor.
- 5 2. The use of the KDR/Flk-1 epitope Y1214 as a marker in the detection of and/or measurement of the level of the KDR/Flk-1 receptor.
3. A probe directed to the KDR/Flk-1 epitope Y1214.
4. A probe according to Claim 3 wherein the probe is an antibody.
5. A method of generating an antibody according to Claim 4, which comprises:
10 (i) immunizing a mammal with a peptide which comprises the KDR/Flk-1 epitope Y1214; and
(ii) isolating an antibody from said mammal.
6. An assay method to measure a change in the activation state of the KDR/Flk-1 receptor utilising Y1214 as a marker.
- 15 7. An assay method for the measurement of a change in the activation state of the KDR/Flk-1 receptor, comprising
(a) mixing a biological sample with an assay mixture comprising one or more probes directed to the KDR/Flk-1 epitope, Y1214 ; and
(b) measuring a signal which is proportional to the proportion of the KDR/Flk-1
20 epitope, Y1214 which is in the phosphorylated or un-phosphorylated state.
8. A diagnostic kit to detect, measure the levels of, and/or measure a change in the activation state of the KDR/Flk-1 receptor comprising reagents for preparing an assay mixture, comprising a probe directed to the KDR/Flk-1 epitope Y1214 according to Claim 3, and instructions for use thereof.
- 25 9. A method of determining the effective dose of an inhibitor of the KDR/Flk-1 receptor, which comprises:
(a) dosing one or more humans or other mammals with a range of KDR/Flk-1 receptor inhibitor concentrations;

-17-

- (b) isolating a biological sample from said humans or other mammals;
 - (c) measuring a signal proportional to the activation state of the KDR/Flk-1 receptor using an assay method according to Claim 6; and
 - (d) calculating the effective dose of the inhibitor from the measured signal.
- 5 10. A method of preparing a pharmaceutical composition of a KDR/Flk-1 receptor inhibitor which comprises:
- (a) determining the effective dose of the inhibitor according to Claim 9; and
 - (b) preparing a unit dose of inhibitor comprising an amount of inhibitor within the effective dose range and a pharmaceutically acceptable excipient.
- 10 11. A pharmaceutical composition prepared according to Claim 10.
12. A method of determining whether a chemical compound is an *in-vivo* inhibitor of the KDR/Flk-1 receptor tyrosine kinase activity which comprises, measuring the degree of phosphorylation of Y1214 in a biological sample obtained from a subject to whom said chemical compound has been administered.
- 15 13. The use of the degree of phosphorylation of Y1214 as a surrogate marker of KDR/Flk-1 receptor tyrosine kinase inhibitory activity of a chemical compound.
14. The use of an antibody which binds to the KDR/Flk-1 epitope Y1214 in the manufacture of a medicament.